

Applicant : Paul D. Coleman *et al.*  
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64. The method of claim 63, wherein the two or more antibodies comprise:

- a) an anti-cathepsin D antibody and mAb69;
- b) an anti-TG-3 antibody and mAb69; or
- c) an anti-MC-1 antibody and mAb69.

65. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a cell cycle regulator.

66. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a lysosomal hydrolase.

67. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a kinase.

68. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a phosphatase.

69. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes an apoptosis factor.

70. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a mitochondrial protein.

71. The method of claim 57, wherein the mRNA isolated in step (b) comprises mRNA that encodes a cell stress-related protein.

72. The method of claim 57, wherein the bodily fluid is cerebrospinal fluid and the mRNA isolated in step (b) comprises mRNA that encodes a synaptic marker or a neurotrophic factor.

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73. The method of claim 57, wherein the bodily fluid is blood.

74. The method of claim 57, wherein the bodily fluid is saliva or urine.

75. The method of claim 57, wherein the non-neural tissue is mucosal tissue or skin.

*B2*  
*cont'd*  
~~76.~~ A method for creating a gene profile for a given stage of Alzheimer's disease, the method comprising:

(a) providing a plurality of cells from a non-neural tissue or bodily fluid of a patient who has Alzheimer's disease, the disease being at the given stage; and

(b) determining the level of expression of one or more types of protein expressed by the cells, wherein the level of expression of the protein(s) constitute(s) a gene profile for the given stage of Alzheimer's disease.

77. The method of claim 76, wherein the stage of Alzheimer's disease is determined by obtaining neuronal cells from the patient and viewing at least one of the neuronal cells through a microscope.

78. The method of claim 77, wherein the stage of Alzheimer's disease is determined by the degree to which the neuronal cells, when viewed through the microscope, appear filled with neurofibrillary tangles.

79. The method of claim 78, wherein the stage of Alzheimer's disease is a stage at which the neuronal cells lack frank neurofibrillary tangles.

80. The method of claim 76, wherein the stage of Alzheimer's disease is determined by obtaining neuronal cells from the patient and exposing at least one of the neuronal cells to two or more antibodies.

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81. The method of claim 80, wherein the two or more antibodies comprise:

- a) an anti-cathepsin D antibody and mAb69;
- b) an anti-TG-3 antibody and mAb69; or
- c) an anti-MC-1 antibody and mAb69.

82. The method of claim 76, wherein step (b) comprises exposing proteins expressed by the cells to one or more antibodies.

B<sup>2</sup> cont'd  
83. The method of claim 82, wherein the one or more antibodies specifically bind to a cell cycle regulator, a lysosomal hydrolase, a kinase, a phosphatase, an apoptosis factor, a mitochondrial protein, or a cell stress-related protein.

84. The method of claim 76, wherein the bodily fluid is cerebrospinal fluid and step (b) comprises exposing proteins expressed by the cells to one or more antibodies that specifically bind a synaptic marker or a neurotrophic factor.

85. The method of claim 76, wherein the bodily fluid is blood.

86. The method of claim 76, wherein the bodily fluid is saliva or urine and the non-neural tissue is mucosal tissue or skin.

87. A method for determining whether an individual has Alzheimer's disease and, optionally, the stage to which the disease has progressed, the method comprising:

- (a) providing a plurality of cells from a non-neural tissue or bodily fluid of the individual;
- (b) isolating mRNA from cells in the plurality to produce a heterologous population of mRNAs;
- (c) determining the level of expression of one or more of the mRNAs within the population of mRNAs, wherein the level(s) of expression constitute(s) a gene profile at the given stage of Alzheimer's disease; and

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(d) comparing the gene profile of the individual with a profile obtained by the method of claim 57, wherein substantial similarity between the individual's profile and the patient's profile indicates that the individual has Alzheimer's disease and, if the patient's profile is a unique representation of a given stage of Alzheimer's disease, that the disease has progressed to about the same stage as that of the patient.

88. The method of claim 87, wherein the mRNA isolated from the individual comprises mRNA that encodes a cell cycle regulator, a lysosomal hydrolase, a kinase, a phosphatase, an apoptosis factor, a mitochondrial protein, or a cell stress-related protein.

89. The method of claim 87, wherein the bodily fluid of the individual is cerebrospinal fluid and the mRNA isolated from the individual comprises mRNA that encodes a synaptic marker or a neurotrophic factor.

90. The method of claim 87, wherein the bodily fluid of the individual is blood.

91. The method of claim 87, wherein the bodily fluid of the individual is saliva or urine.

92. The method of claim 87, wherein the non-neural tissue of the individual is mucosal tissue or skin.

93. A method for determining whether an individual has Alzheimer's disease and, optionally, the stage to which the disease has progressed, the method comprising:

- (a) providing a plurality of cells from a non-neural tissue or bodily fluid of the individual;
- (b) determining the level of expression of one or more types of protein expressed by the cells, wherein the level(s) of expression constitute(s) a gene profile for the individual; and
- (c) comparing the gene profile of the individual with a profile obtained by the method of claim 76, wherein substantial similarity between the individual's profile and the patient's profile indicates that the individual has Alzheimer's disease and, if the patient's profile is a unique

B<sup>2</sup> cont'd

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representation of a given stage of Alzheimer's disease, that the disease has progressed to about the same stage as that of the patient.

94. The method of claim 93, wherein the protein expressed by the cells of the individual comprises a cell cycle regulator, a lysosomal hydrolase, a kinase, a phosphatase, an apoptosis factor, a mitochondrial protein, or a cell stress-related protein.

95. The method of claim 93, wherein the bodily fluid of the individual is cerebrospinal fluid and the protein isolated from the individual comprises a synaptic marker or a neurotrophic factor.

96. The method of claim 93, wherein the bodily fluid of the individual is blood.

97. The method of claim 93, wherein the bodily fluid of the individual is saliva or urine.

98. The method of claim 93, wherein the non-neural tissue of the individual is mucosal tissue or skin.

99. A method for determining whether a compound affects the gene profile for a given stage of Alzheimer's disease, the method comprising:

- (a) creating a gene profile according to the method of claim 57 for
- (i) a first patient who has Alzheimer's disease, the disease being at the given stage, the first patient having been treated with the compound and
  - (ii) a second patient who has Alzheimer's disease, the disease being at the given stage, the second patient being one who has not been treated with the compound; and
- (b) comparing the gene profile created for the first patient with the gene profile created for the second patient, a difference in the profiles of the first and second patients indicating that the compound affects the profile of genes expressed at the given stage of Alzheimer's Disease.

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100. A method for determining whether a compound affects the gene profile for a given stage of Alzheimer's disease, the method comprising:

(a) creating a gene profile according to the method of claim 76 for

(i) a first patient who has Alzheimer's disease, the disease being at the given stage, the first patient having been treated with the compound and

(ii) a second patient who has Alzheimer's disease, the disease being at the given stage, the second patient being one who has not been treated with the compound; and

(b) comparing the gene profile created for the first patient with the gene profile created for the second patient, a difference in the profiles of the first and second patients indicating that the compound affects the profile of genes expressed at the given stage of Alzheimer's Disease.--

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